Robust Mode Analysis of VCD Spectra: How Reliable are VCD Spectra?

Patrick Bultinck

Department of Inorganic and Physical Chemistry, Ghent University, Krijgslaan 281 (S3), 9000 Gent, Belgium. Patrick.Bultinck@UGent.be

Vibrational circular Dichroism (VCD) is one of the most promising techniques to establish the absolute configuration of chiral molecules. Because of some important advantages compared to most other techniques that allow determination of absolute configuration, it has become a popular tool in especially pharmaceutical industry.
Good algorithms have been implemented for the calculation of VCD spectra using ab initio methods. The assignment of the absolute configuration is then done by, usually simple, comparison between theory and experiment. However, given the stakes in this industry, VCD assisted assignment of the absolute configuration must be done with greatest care, justifying the need to examine many different factors that influence the agreement between experiment and theory.
In this lecture we will address some, until recently *hidden*, factors that can influence heavily the conclusions drawn from comparing theory and experiment. The two main questions that will be addressed are:

1. Is every peak in a VCD spectrum sufficiently reliable for use in assignment of the absolute configuration or can only robust modes be used ? [1]
2. Can agreement between spectra be expressed in some mathematical form such that rather than a *feeling* for the degree of similarity, the similarity can be expressed in some number. [2]

For question 1, we will discuss the idea of robust modes, relying on the angle extended between the electric and magnetic transition dipole moments. For question 2, we will discuss some simple overlap integrals between theoretical and experimental spectra.

[1] Nicu, V.P.; Debie, E.; Herrebout, W.; Van der Veken, B.; Baerends, E.J.; Bultinck, P. A robust mode analysis of transfer of chirality in VCD: the case of pulegone in chloroform. Chirality, 2010, 21, E287-E297.
[2] Kuppens, T., Langenaeker, W.; Tollenaere, J.P.; Bultinck, P.; Determination of the Stereochemistry of 3-Hydroxymethyl-2,3-Dihydro-[1,4]Dioxino[2,3-B]Pyridine by Vibrational Circular Dichroism and the Effect of DFT Integration Grids, J. Phys. Chem., 2003, 107, 542-553.